AMRL-TDR-63-3

THE PATHOPHYSIOLOGY OF DISUSE AND THE PROBLEM OF PROLONGED WEIGHTLESSNESS: A REVIEW

MICHAEL McCALLY, CAPTAIN, USAF, MC

BIOMEDICAL LABORATORY
6570th AEROSPACE MEDICAL RESEARCH LABORATORIES

RICHARD W. LAWTON, M.D.

GENERAL ELECTRIC COMPANY
PHILADELPHIA 4, PENNSYLVANIA

TECHNICAL DOCUMENTARY REPORT No. AMRL-TDR-63-3

JUNE 1963

6570th AEROSPACE MEDICAL RESEARCH LABORATORIES
AEROSPACE MEDICAL DIVISION
AIR FORCE SYSTEMS COMMAND
WRIGHT-PATTERSON AIR FORCE BASE, OHIO

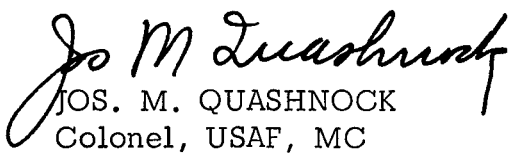
Project No. 7222, Task No. 722201

ABSTRACT

The physiological implications of zero-G as encountered in space flight are discussed and the available research concerning the physiological effects of weightlessness is reviewed. The purpose of this review is to proceed from the present state of knowledge of normal human physiological systems, particularly as their structure and function are affected by gravity, to a consideration of the possible physiological consequences of prolonged human exposure to zero-G. Methods used to produce and to simulate zero-G are briefly reviewed. The data suggesting that prolonged weightlessness will be a deconditioning environment is presented. This data is considered for possible untoward effects of prolonged exposure to weightlessness, and for methods of prevention of undesired effects. The problem of artificial gravity by rotation of a space vehicle is briefly considered. Areas of needed future investigation are suggested.

PUBLICATION REVIEW

This technical documentary report has been reviewed and is approved.



JOS. M. QUASHNOCK
Colonel, USAF, MC
Chief, Biophysics Laboratory

TABLE OF CONTENTS

THE PATHOPHYSIOLOGY OF DISUSE AND THE PROBLEM OF PROLONGED WEIGHTLESSNESS: A REVIEW

''Just as we are accustomed to think of the physiology of exercise, we should be thinking about the pathology of inactivity and disuse.''

J. N. Morris
1959

I. INTRODUCTION

As long as man has contemplated space flight his imagination has been captured by the state of zero-gravity (zero-G) or weightlessness. In this area of biological unknowns speculation has often outstripped the collection of data. As the zero-G state cannot yet be effectively created or maintained for more than brief seconds on earth, the physiological effects of prolonged weightlessness remain unknown.

Information regarding weightlessness is, in general, of four types:

a. Data is available from the exposure of man and animals to brief periods of zero-G in drop towers, aircraft flying Keplerian parabolas, and ballistic missiles.

b. Other data has been taken from situations thought to bear some physiological analogy to weightlessness —— such as recumbency, immobilization, and water immersion.

c. A large part of present thinking on the subject of weightlessness is speculation about the functions of known physiological systems in the absence of gravity.

d. Physiological data is now available from manned space flight itself.

Design criteria for future manned space vehicles depend heavily upon adequate experimental biological data that can be obtained only in space. This data may be collected using two general approaches, both of which have their advocates. First, man's exploration of space may proceed in small increments of duration and distance as exemplified by the X-15 and Mercury programs. Extension of the period of weightlessness will be achieved a step at a time with biological, engineering, operational, and safety factors assessed simultaneously. The second or large-increment approach, exemplified by the Russian experiment with the dog Laika, would orbit suitably instrumented animals for prolonged periods. Here, weightlessness or other biological effects of prolonged space flight could be studied relatively undistracted by the operational and engineering aspects of a manned vehicle. Information could be obtained well in advance of the manned space program. The early acquisition of such data appears mandatory for the realistic planning of extended manned orbital and lunar missions.

The results of animal (refs. 1, 2) and manned orbital space flights (refs. 3, 4) to date suggest that weightlessness itself is tolerable and perhaps even pleasant, at least for a few hours. The most important and completely unstudied problem is that of the cumulative, time-dependent, and adaptive changes of prolonged exposure. It has been suggested (refs. 5, 6) that prolonged exposure to zero-G will produce deconditioning of physiological systems and that such deconditioning in an environment of reduced or absent gravitational force may seriously impair man's ability to tolerate normal or increased G-forces following this exposure. Conditioning is the adaptation of an organism to its particular environment or way of life. The human is an extremely adaptive organism which quickly adjusts itself to the demands or lack of demand placed upon it. The sedentary desk worker is physiologically far removed from a lumberjack and the pearl diver has biological mechanisms unknown to the high-altitude dweller. Deconditioning is the adaptation of an organism to a less demanding environment. An excellent example is the physiological alteration produced by bed rest. Consider the difference in the performance of a well-trained athlete before and immediately after 6 weeks of strict bed rest. Deconditioning may be defined as the sum of the difference in measurements made before and following exposure to a less demanding environment. This concept has recently been discussed in terms of cybernetic theory (ref. 7).

Much literature on various aspects of the problem of weightlessness has accumulated in a short period. A number of pertinent reviews is available. The early history of the weightlessness problem, principally as studied by means of Keplerian parabolas in aircraft at the USAF School of Aerospace Medicine, Brooks AFB, Texas, has been reviewed by Campbell and Gerathewohl (ref. 8). A historical review of a variety of

weightlessness studies performed at Holloman AFB, New Mexico, between 1948 and 1958 is also available, including a brief review of the pioneer studies of the German workers Diringshofen, Strughold, Haber, and Gauer (ref. 9). Aeronautical Systems Division studies in weightlessness using aircraft have recently been reviewed (refs. 10, 11). Weightlessness and performance has been reviewed by Loftus and Hammer (ref. 12). An annotated bibliography, Animals and Man in Space, by Beischer and Fregly is a useful reference to data collected in suborbital and orbital space flight (ref. 3). Henry and his coworkers have recently reviewed the biological effects of the weightlessness state as determined in ballistic suborbital and orbital space flights by the United States and Russia (ref. 4). Lawton has reviewed the biological implications of weightlessness in relation to normal physiological mechanisms (ref. 13). Zero-G devices and simulators have been reviewed by Gerathewohl (ref. 14).

The purpose of this review is to proceed from the present state of knowledge of normal human physiological systems, particularly as their structure and function are affected by gravity, to a consideration of the possible physiological consequences of prolonged exposure to zero-G. Methods used to produce and simulate zero-G will also be briefly reviewed. The data that suggests that weightlessness will be a deconditioning environment is presented. This data is considered for suggestions as to the possible untoward effects of prolonged exposure to weightlessness and for methods of protection from and prevention of undesired effects. The problems associated with artificial gravity by rotation of the space vehicle —— in particular, vestibular stimulation —— are also briefly considered.

I. LIST OF REFERENCES

1. Burch, G.E., and S.J. Gerathewohl, "Observations on Heart Rate and Cardiodynamics during Weightlessness," Aerospace Med. 31:661, 1960.

2. Kousnetzov, A.G., "Some Results of Biological Experiments in Rockets and Sputnik II," J. of Aviat. Med. 29:781, 1958.

3. Beischer, D.C., and A.R. Fregly (Editors), Animals and Man in Space. A Chronology and Annotated Bibliography through the Year 1960, ONR Report ACR - 64, Office of Naval Research, Washington 25, D.C., 1960.

4. Henry, J.P., "Effects of Weightlessness in Ballistic and Orbital Flight. A Progress Report," Aerospace Med. 33:1056, 1962.

5. Graybiel, A., and B. Clark, "Symptoms Resulting from Prolonged Immersion in Water. The Problem of Zero-G Asthenia," Aerospace Med. 32:181, 1961.

6. Graveline, D.E., B. Balke, R.E. McKenzie, and B. Hartman, "Psychobiological Effects of Water-Immersion-Induced Hypodynamics," Aerospace Med. 32:387, 1961.

7. Stanley-Jones, D. and K. The Kybernetics of Natural Systems, Pergamon Press, New York, 1960.

8. Campbell, P.A., and S.J. Gerathewohl, "The Present Status of the Problem of Weightlessness," Texas State J. of Med. 55:267, 1059.

9. AFMDC History of Research in Subgravity and Zero-G at the Air Force Missile Development Center: 1948-1958, Office of Information Services, Holloman Air Force Base, New Mexico, 1958.

10. ARDC Zero Gravity Survey, Directorate of Advanced Systems Technology, Wright Air Development Division, Wright-Patterson Air Force Base, Ohio, 1960.

11. Hammer, Lois R., Aeronautical Systems Division Studies in Weightlessness: 1959-1960, WADD TR 60-715, Wright Air Development Division, Wright-Patterson Air Force Base, Ohio, 1961.

12. Loftus, J.P., and Lois R. Hammer, Weightlessness and Performance: A Review of the Literature, ASD TR 61-166, Aeronautical Systems Division, Wright-Patterson Air Force Base, Ohio, 1961.

13. Lawton, R., "Physiologic Considerations Relevant to the Problem of Prolonged Weightlessness: A Review," Astronaut. Sci. Rev. 4:1, 1962.

14. Gerathewohl, S.J., Zero-G Devices and Weightlessness Simulators, Publication 781, National Academy of Sciences - National Research Council, Washington, D.C., 1961.

II. METHODS IN THE STUDY OF ZERO-G

A true agravic condition occurs only in the complete absence of gravitational force, while zero-G is produced when the accelerative force of gravity on an object is vectorially opposed by an inertial force. In an orbiting space vehicle, the force of gravity is opposed by an opposite and equal centrifugal force, resulting in zero-G or weightlessness. The concept of weight and the physics and terminology of zero-G have been discussed at length and are not reviewed here (refs. 1, 2). A few conceptual subtleties are worthy of note, however. Schaefer has emphasized that zero-G, in an orbiting vehicle of finite dimensions, prevails only at the vehicle's center of gravity (ref. 3). At any other point the balance of centrifugal force and gravitational attraction is incomplete and a sub-gravity (sub-G) state exists. Although this difference is minute, the cumulative consequences may be many in terms of vestibular stimulation and its effect on crew performance. Secondly, this nonhomogeneity of field forces may give rise to intracellular forces so that a real nonidentity of the biological effects of the agravic and the zero-G conditions exists. For this discussion zero-G and sub-G are considered synonymous, as the biological effects of sub-G presumably differ from those of zero-G only in the time course with which they develop.

Aircraft flying Keplerian parabolas have probably provided the greatest quantity of data regarding the biological effects of weightlessness. These studies have shown that man can function in a brief weightlessness state without gross physiological or psychomotor disturbance, dispelling many uncertainties and fears. The type of data provided by this method is severely limited by the short duration of exposure to weightlessness (14 to 45 seconds depending on the type of aircraft used) and by the presence of up to 3 G's immediately before and following the period of weightlessness. This method will continue to be useful in physical and engineering studies and in the training and selection of astronauts.

Using experimental animals in ballistic missiles was an early source of information regarding the biological effects of weightlessness and radiation. In the late 1940's Henry et al. showed that sedated monkeys exposed to zero-G for periods of approximately 2 minutes in the nose of an Aerobee rocket showed no significant changes in arterial or venous blood pressure or heart rate (ref. 4). The Russians have been very productive in the study of experimental animals in zero-G, culminating their efforts with the orbital flight of the dog Laika in Sputnik II on 3 November 1957 (ref. 5). This study showed that mammals could satisfactorily survive conditions approaching those of space flight, including zero-G.

The physical states of recumbency, inactivity, and water immersion are presently being reinvestigated. With regard to certain physiological systems, these states may be regarded as analogues of weightlessness. An analogy is an implied comparison. To extend data obtained from the study of bed rest or water immersion to zero-G involves assumptions about the nature of weightlessness. Such analogies must be made cautiously.

Bed rest has been evaluated with a wide variety of subjects including normal individuals, comatose patients, patients with spinal cord damage and paralysis, and patients seriously debilitated with catabolic disease. Complications of bed rest that have been studied in clinically ill patients include phlebothrombosis and pulmonary embolism, hypostatic pneumonia, decubitus ulcers, nephrolithiasis, constipation, muscle atrophy, osteoporosis, and orthostatic hypotension. These undesirable effects of bed rest have raised fundamental questions concerning the convalescence and rehabilitation of the medically ill, and have contributed to the present practice of early postoperative ambulation. In recumbency, the hydrostatic pressure effects of body fluids are minimized by reducing the height of the hydrostatic column to approximately one-seventh of its value erect. The circulatory system of a recumbent man thus approaches the gravity-free condition. A significant redistribution and mobilization of body fluids occurs when assuming the recumbent posture. A decrease in the general metabolic rate, as compared to the erect posture, occurs. These characteristics of recumbency have stimulated a wide variety of studies of the relationships of gravity, posture, and activity to the normal functions of physiological systems.

Water immersion of human subjects has been suggested as a convenient simulator or analogue of weightlessness (ref. 6). A body immersed in a fluid of the same density is, in effect, weightless as the gravitational force applied to the body is opposed by a force equal to the mass of the displaced fluid. In the immersion situation the hydrostatic pressure of the body fluids due to gravity is counterbalanced by the equal hydrostatic pressure of the immersion fluid outside of the body. Redistribution of body fluids (ref. 7), orthostatic hypotension (ref. 8), decreased demands for musculoskeletal activity, decreased metabolic rate (ref. 9), and catabolism (ref. 10) are produced by water immersion as well as by bed rest, so that both are useful analogies to weightlessness. In many important aspects the analogy of weightlessness and immersion is faulty. In immersion the subject is still acted upon by gravity field forces at the interfaces of tissues of different densities, such as gas-filled cavities and the otolith organ of the utricle.

The body is also surrounded by water rather than air and significant inertial forces due to the resistance of the water are generated when the subject moves. A pressure gradient proportional to depth may exist in certain experimental immersion situations, producing significant respiratory and cardiovascular alterations. Water immersion of human subjects with a variety of techniques has been used to study cardiovascular dynamics (ref. 11), spatial orientation (ref. 12), sensory deprivation (ref. 13), acceleration protection (ref. 14), and, more recently, the problem of zero-G deconditioning or asthenia (refs. 8, 10).

Another approach to weight- or gravity-dependent biological phenomena is the study of small animals exposed to prolonged positive acceleration by continual centrifugation (refs. 15, 16, 17, 18). Such animals, studied after months of continuous exposure to 2.5 to 4 G's, show an increase in the relative mass of their diaphragms, gastrocnemius muscles, and in the weight and length of the femur and other weight-supporting bones, when compared to litter mate controls (ref. 15). Heart rate and hematocrit increase and respiratory rate decreases in chickens centrifuged for 3 to 7 weeks at 4 G's (ref. 16). While the structural and functional differences observed between animals exposed to 1 and 2 G's cannot necessarily be extrapolated to describe differences between 1 and 0 G, the rate of atrophy and catabolism in biological systems in animals brought suddenly from a hypergravic to a normal gravity environment may suggest the time course of disuse changes in weightlessness.

All weightlessness devices and analogues to date are imperfect and physiological data obtained from their use can be related to the condition of zero-G only with great caution. The effects of inactivity, characteristic of experiments involving bed rest, confinement, and immersion should not be confused with possible effects of weightlessness per se. Thus, bed rest and immersion are not necessarily realistic analogues of the weightlessness that will be experienced aboard a spacecraft in which crew members will be physically active, performing their assigned functions.

On the other hand, the effects of prolonged weightlessness on man are not known, and these effects may be such as to cause serious physiological or psychomotor impairment, especially following prolonged exposure. Only by extending our knowledge of the basic physiological mechanisms involved in anti-G compensation will we be able to define and predict these effects and devise the appropriate protective devices or techniques necessary to each new space operation. Indeed, space flight offers the opportunity to explore the terrestrial gravity dependence of biological function to which man has so long been adapted.

II. LIST OF REFERENCES

1. Margaria, R., "Wide Range of Investigations of Acceleration in Man and Animals," J. of Aviat. Med. 29:855, 1958.

2. Ritter, O.L., and S.J. Gerathewohl, The Concept of Weight and Stress in Human Flight, Report No. 58-154, USAF School of Aviation Medicine, Randolph AFB, Texas, 1959.

3. Schaefer, H.J., A Note on the Gravity-Free State on a Space Platform, Research Project NM 17-01-11 Report No. 48, USN School of Aviation Medicine, Pensacola, Florida, 1959.

4. Henry, J.P., E.R. Maher, and D.G. Simons, "Animal Studies of the Sub-Gravity State during Rocket Flight," J. Aviat. Med. 23:421, 1952.

5. Kousnetzov, A.G., "Some Results of Biological Experiments in Rockets and Sputnik II," J. Aviat. Med. 29:781, 1958.

6. Knight, L.A., "An Approach to the Physiological Simulation of the Null-Gravity State," J. Aviat. Med. 29:283, 1958.

7. Graveline, D.E., and Margaret M. Jackson, "Diuresis Associated with Prolonged Water Immersion," J. App. Physiol. 17:519, 1962.

8. Graybiel, A., and B. Clark, "Symptoms Resulting from Prolonged Immersion in Water. The Problem of Zero G Asthenia," Aerospace Med. 32:181, 1961.

9. Donald, K.W., and W.M. Davidson, "Oxygen Uptake of Booted and Fin Swimming Divers," J. Applied Physiol. 7:31, 1954.

10. Graveline, D.E., B. Balke, R.E. McKenzie, and B. Hartman, "Psychobiological Effects of Water-Immersion-Induced Hypodynamics," Aerospace Med. 32:387, 1961.

11. Hellebrandt, F.A., and E. Brogdon, "The Hydrostatic Effect of Gravity on the Circulation in Supported, Unsupported and Suspended Postures," Am. J. Physiol. 123:95, 1938.

12. Brown, J.L., "Orientation to the Vertical during Water Immersion," Aerospace Med. 32:209, 1961.

13. Lilly, J.C., "Mental Effects of Physical Restraint and of Reduction of Ordinary Levels of Physical Stimuli on Intact, Healthy Persons," Psychiat. Res. Rep. 5:1, 1956.

14. Bondurant, S., W. G. Blanchard, and N.P. Clarke, Effect of Water Immersion on Human Tolerance to Forward and Backward Acceleration, WADC TR 58-290, Wright Air Development Center, Wright-Patterson Air Force Base, Ohio, 1958.

15. Briney, S.R., and C.C. Wunder, "Growth of Hamsters during Continual Centrifugation," Am. J. Physiol. 202:461, 1962.

16. Smith, A.H., C.M. Winget, and C.F. Kelly, Physiologic Effects of Artificial Changes in Weight, Naval Res. Rev. 16-24, Washington 25, D. C., April 1959.

17. Smith, A.H., C.M. Winget, and C.F. Kelly, "Growth and Survival of Birds under Chronic Acceleration," Growth 23:97, 1959.

18. Wunder, C.C., "Survival of Mice during Chronic Centrifugation. I. Studies of Male Mice at Different Ages at Onset of Exposure to One Field and Those at Different Intensities of Gravity for Animals of the Same Age," Aerospace Med. 33:866, 1962.

III. GENERAL METABOLIC EFFECTS

There appears to be a clear-cut relationship between metabolism and gravity. The metabolic costs of passive standing were demonstrated by Tepper and Hellebrandt who, in a study of 75 young women, found a metabolic increment between recumbency and passive standing on a tilt table of +5.71 calories/square meter/hour or 16.25% (ref. 1). In 31 experiments on 12 healthy young women, Turner, Newton, and Haynes found an increment of +5.8% at 62° tilt and 19% at 90° (ref. 2). The increase in metabolism on passive standing arises presumably from gravity stimulation of proprioceptors in muscles and joints with increased anti-gravity (anti-G) or extensor muscle tonus. Crowden reported a marked reduction in oxygen requirements for exercise in water compared to air in a single subject (ref. 3). Hill confirmed this work and pointed out that buoyancy in water reduces the amount of work against gravity (ref. 4). Donald and Davidson have also suggested that reduced postural effort may account for the near basal oxygen consumption they observed in submerged sitting subjects at 70° F (ref. 5). The important variables of water temperature and subject work were not measured in the Crowden and Hill studies. More recently, Goff et al. measured the oxygen uptake of four subjects at rest and during mild exercise in air and completely immersed in water at 29.5° to 36.5° C and found that for isometric workloads, including rest, there was no significant change in metabolic rate between dry and submerged tests (ref. 6).

The relationship between metabolic rate and postural muscle activity suggests that the basal metabolism of weightlessness may be closely related to that of recumbency, inactivity, or immersion. However, the differences in basal metabolism between recumbency and quiet standing are small in comparison with the metabolic costs of exercise. Energy costs for self-propulsion under weightlessness may be high until coordinated body movements are achieved by practice.

In a spacecraft free motion may be limited, thus reducing exercise. If space suits and restraint systems are used and crew tasks are principally observation and monitoring, there may be a need for programmed exercise. Confinement and inactivity will undoubtedly be characteristic of space flight, but it is not possible at the present to separate the metabolic effects related to inactivity from those which might be due to weightlessness. Oxygen consumption estimated from caloric intake in two subjects confined for long periods (17 and 30 days) in the School of Aerospace Medicine space cabin simulator indicates near basal (360 liters/24 hours) oxygen consumption for such "space equivalent" exposure (ref. 7).

L 882-63
AMD/AFFTC/AFMDC/APGC--DD

21 AUG 196 1C
ASTAR NO. 5032 9A
(UNEDITED)

ASTAR NO. 5032 JUNE 20TD-BDS,TD-BX,TD-E,TD-EEC,TD-EEO,TD-ES,TD-F,
NIKOLAY FILIMONOV. M.D. TD-FSF,TD-H,TD,SPAO
QUOTE IN THE STATE OF WEIGHTLESSNESS UNQUOTE.
T-4120 TRUD, JUNE 18, 1963, PAGE 3, COLUMNS 5 TO 7.

VARIOUS WAYS OF /COUNTERACTING THE EFFECTS OF LONG PERIODS OF WEIGHTLESSNESS/ ARE USED DURING THE SPACE FLIGHT. TO FORCE THE HEART TO PERFORM NORMALLY IN A CONDITION WHERE THE ORGANISM IS IN A STATE OF QUOTE HYPODYNAMICS UNQUOTE, PNEUMATICALLY INFLATED CUFFS ARE PLACED ON THE EXTREMITIES OF THE ASTRONAUT. BY PERIODICALLY INFLATING THOSE CUFFS AND COMPRESSING THE CORRESPONDING BLOOD VESSELS, ARTIFICIAL LOADS ON THE CARDIOVASCULAR SYSTEM ARE CREATED WHICH FORCE THE HEART TO OVERCOME THE LOADS AND TO CONTRACT MORE ENERGETICALLY. MUSCULAR EXERCISES ARE ALSO VERY HELPFUL, PARTICULARLY IF THE MUSCLES ARE PERFORMING ALL THE MOVEMENTS TO WHICH THEY ARE DESTINED. SO FOR EXAMPLE THE ARM AND HAND EXERCISES SHOULD NOT ONLY INCLUDE MOVEMENTS INCREASING THE STRENGTH AND ENDURANCE OF THE MUSCLES, BUT ALSO EXERCISES SERVING TO PRESERVE THE COORDINATION OF THE MOVEMENTS. THE MUSCULAR ACTIVITY DURING THE SPACE FLIGHT USUALLY INCREASES THE ACTION OF THE CARDIOVASCULAR SYSTEM AND OF THE VESTIBULAR APPARATUS, THE COMBINATION OF THE PRE-FLIGHT TRAINING AND THE IN-FLIGHT EXERCISES ENHANCES THE WELL-BEING AND THE WORK CAPABILITIES OF THE ASTRONAUT.

20 JUN 63 07 19

1/1 lm/kes 449 79, 356

L 904-63
AMD/AFFTC/AFMDC/ESD-3

21 AUG 196
ASTAR NO. 5038
(UNEDITED)

ASTAR NO. 5038 JUNE 27
SPECIAL. TD-BDS-TO-BX-TD-E-TD-EEC
NEPSZABADSAG, BUDAPEST, JUNE 20, 1963. TD-EED-TO-F, TD-H, TD-SPAO

ERNEO NAGY, SECRETARY OF THE HUNGARIAN ASTRONAUTICAL SOCIETY, SAYS HIS ASSUMPTION THAT BOTH /VOSTOK 5 AND 6/ WOULD LAND EITHER ON JUNE 19 OR 20TH BETWEEN 9.00 A.M. AND 1.00 P.M. WAS JUSTIFIED BECAUSE ONLY THREE ORBITS COVERING THE NORTHEASTERN PART OF THE USSR WERE SUITABLE FOR LANDING. THE CAPSULES WERE ABLE TO DESCEND OVER THE WIDE REACHES OF THE ADJOINING SOVIET TERRITORY AND WERE IN FULL REACH OF THE SOVIET RADIO AND RADAR STATIONS.
THE SPEED OF THE CAPSULES IS BRAKED BY THE RETRO-ROCKETS FROM 7,850 TO 7,600 METERS PERSECOND. LANDING PATH OF THE VOSTOKS INDICATE THAT THE RESISTANCE OF THE CAPSULE IS ALTERED DURING THE LANDING MANEUVER, AND THE SPEED IS REDUCED FROM 7,600 M/SEC TO 300 - 400 M/SEC. AN QUOTE AIRY UNQUOTE PARACHUTE OPENS AND ARRESTS THE FREE FALL OF THE CAPSULE. AT AN ALTITUDE OF 6 - 7 KILOMETERS THE BIG PARACHUTE OPENS AND BRINGS THE CAPSULE SAFELY TO EARTH. THE IMPACT ON THE GROUND IS SOFTENED BY CUSHIONS WHICH FILL WITH AIR DURING THE DESCENT. THE COSMONAUTS DECIDE AT AN ALTITUDE OF 3 - 4 KILOMETERS WHETHER THEY WANT TO BAIL OUT AND PARACHUTE TO EARTH OR REMAIN IN THE CAPSULE. AS A NATURAL REACTION OF THE LONG STAY IN THE CAPSULE, MOST COSMONAUTS CHOOSE THE FIRST ALTERNATIVE.

27 JUN 63 10 00

1/1 lm/kes 1C 9A #66

In a now classical study of bed rest by Deitrick, Whedon, and Shorr, four normal healthy young men were immobilized in bivalved casts from the umbilicus to the toes for 6 to 7 weeks following suitable control periods on a constant dietary intake (ref. 8). Under these circumstances a decline of 6.9% in metabolic rate occurred. Total nitrogen losses averaged 53.6 grams for the 6-week immobilization period and were associated with a lowered creatine tolerance and a decrease in muscle mass and strength most marked in the immobilized leg muscles. Total calcium loss for 6 weeks of immobilization and 3 weeks of recovery ranged from 9.0 to 23.9 grams. The calcium content of the urine was doubled and this —— together with the absence of an appreciable rise in urine volume, a slight rise in urinary pH, and the failure of urinary citric acid to rise parallel with the calcium —— favored the precipitation of calcium phosphate although stone formation was not detected. Deterioration in the mechanisms essential for adequate circulation in the erect posture was grossly apparent as a tendency for subjects to faint during tilt table tests. This orthostatic intolerance was prevented by elastic binders applied to the legs before tilt. Blood volume diminished an average of 5.4% during the bed rest period, exercise tolerance decreased, and resting pulse rate increased 3.8 beats per minute. Complete recovery of normal metabolic and physiological functions required 3 to 4 weeks. In the case of an astronaut, no such severe changes are expected, but the physiological effects of confinement and restricted activity must be considered additive with those of weightlessness.

Graveline et al. at the USAF School of Aerospace Medicine studied the psychophysiological responses of a single subject (Graveline) immersed in water (ref. 9). In this experiment the subject wore a dry-type rubber suit of conventional SCUBA (self-contained underwater breathing apparatus) design and was immersed semirecumbent with his head out for 7 days with the exception of brief daily periods of emersion for electrode change and skin hygiene. Unfortunately, only a single subject was used, the preimmersion control period was brief, and daily fluid intake during immersion was not recorded. Blood morphology, ECG, blood pressure, heart rate, EEG, urine volume, blood and urine electrolyte levels, and psychomotor proficiency were measured. The subject reported progressively increasing weakness and fatigue, during the emersed periods only, which necessitated termination of the experiment after 7 days. The metabolic rate remained unchanged. The white blood count rose from 7,000 to 15,000. The 24-hour urine output was double the control value for the first 3 days of the test and was associated with large urinary nitrogen losses.

Minor changes in calcium excretion occurred. A comparison of preimmersion and postimmersion work capacity, orthostatic tolerance, and G-tolerance was made. All measurements paralleled those expected in the light of bed rest data, but the changes were early and marked. Centrifuge tests demonstrated a decline in acceleration ($+G_z$) tolerance as indicated by heart rate but not by "blackout" tolerance. The subject was flown from San Antonio, Texas, to Wright-Patterson Air Force Base, Ohio, for the G-tolerance studies and some recovery of normal function may have occurred. Measurements of transverse ($+G_x$) tolerance would also have been more desirable than headward ($+G_z$) acceleration tolerance if such data is to be applied to present space programs.

Beckman and coworkers have also studied the biological effects of water immersion (ref. 10). Their results with regard to head-out immersion are qualitatively identical with those of Graveline et al. (ref. 9). In the situation of water immersion to the level of the neck the hydrostatic pressure of the immersion fluid produces an equivalent of negative pressure breathing. Beckman et al. reviewed the known physiological effects of negative pressure breathing including changes in pulmonary volumes, cardiac index, and urine flow. They concluded that many of the changes observed during and following head-out immersion were related to the hydrostatic pressure of the immersion fluid on the chest. In a subsequent report the same authors studied the response to positive acceleration of 12 experienced Navy SCUBA divers following 18 hours of complete immersion. Slight positive pulmonary pressure from the SCUBA regulator was used. The diuretic response to immersion was prevented, and a small but statistically significant decrease in the G-level at which limitation of ocular motility (a test for $+G_z$) tolerance) occurred was noted (ref. 11).

Graybiel and Clark used a combination of 10 hours a day of immersion and the remainder of bed rest in a 2-week study of 3 subjects (ref. 12). No significant changes in muscle strength, exercise tolerance, or psychomotor performance occurred. However, marked orthostatic hypotension, which persisted for 48 hours after the conclusion of the immersion, was demonstrated on the tilt table during and following the immersion period.

Studies of bed rest and water immersion of human subjects demonstrate that disuse may cause deconditioning or impairment of function of a number of physiological processes and reflexes. In the weightlessness state there will no doubt be decreased demands for musculoskeletal support, and for cardiovascular postural reflexes, as well as altered proprioceptive sensory input to the central nervous system.

Disuse of a variety of physiological systems seems a likely consequence of prolonged weightlessness. Thus, physiological changes similar to those produced by bed rest and water immersion are likely. The assumptions made in these analogies remain to be tested in the space environment.

III. LIST OF REFERENCES

1. Tepper, R.H., and F.A. Hellebrandt, "The Influence of the Upright Posture on the Metabolic Rate," Am. J. Physiol. 122:563, 1938.

2. Turner, A.H., M.I. Newton, and F.W. Haynes, "The Circulatory Reaction to Gravity in Healthy Young Women," Am. J. Physiol. 94:507, 1930.

3. Crowden, G.P., "The Relative Energy Expenditure in Muscular Exercises Performed in Air and Water," J. Physiol. 84:31P, 1935.

4. Hill, L., "Exercises in the Bath," Brit. Med. J. II:1153, 1950.

5. Donald, K.W., and W.M. Davidson, "Oxygen Uptake in Booted and Fin-Swimming Divers," J. Appl. Physiol. 7:31, 1954.

6. Goff, L.G., H.F. Bruback, H. Specht, and N. Smith, "The Effect of Total Immersion at Various Temperatures on Oxygen Uptake at Rest and during Exercise," J. Appl. Physiol. 9:59, 1956.

7. Welch, B.E., T.E. Morgan, Jr., and F. Ulvedal, "Observations in the SAM Two-Man Space Cabin Simulator. I. Logistical Aspects," Aerospace Med. 32:583, 1961.

8. Deitrick, J.E., G.D. Whedon, and E. Shorr, "Effects of Immobilization upon Various Metabolic and Physiological Functions of Normal Men," Am. J. Med. 4:3, 1948.

9. Graveline, D.E., B. Balke, R.E. McKenzie, and B. Hartman, "Psychobiological Effects of Water-Immersion-Induced Hypodynamics," Aerospace Med. 32:387, 1961.

10. Beckman, E.L., K.R. Coburn, R.M. Chambers, R.E. DeForest, W.S. Augerson, and V.G. Benson, "Physiologic Changes Observed in Human Subjects during Zero G Simulation by Immersion in Water up to Neck Level," Aerospace Med. 32:1031, 1961.

11. Benson, V.G., E.L. Beckman, K.R. Coburn, and R.M. Chambers, "Effects of Weightlessness as Simulated by Total Body Immersion upon Human Response to Positive Acceleration," Aerospace Med. 33:198, 1962.

12. Graybiel, A., and B. Clark, "Symptoms Resulting from Prolonged Immersion in Water. The Problem of Zero-G Asthenia," Aerospace Med. 32:181, 1961.

IV. BODY FLUIDS

In both standing and recumbency a significant redistribution of body fluids occurs. The hydrostatic pressure of body fluids due to gravity exerts considerable effect during changes in posture, especially on the vascular compartment. Compensatory adjustments are required to maintain an optimum balance between the volume of the circulatory system and other body fluids. In subjects changing from recumbency to standing, Thompson et al. noted a loss of protein-free fluid from the blood, probably due to increased capillary pressure (ref. 1). This amounted to 11% of the total plasma volume. Using the carbon monoxide method of blood volume determination, Waterfield observed a 15% decrease in total plasma volume after 40 minutes of quiet standing (ref. 2). Epstein et al. also reported a decrease in plasma volume during standing. In addition, he described a fall in renal plasma flow, glomerular filtration rate (GFR), and excretion of water and sodium (ref. 3).

Conversely, in the recumbent position, the hydrostatic column of blood due to gravity is diminished to approximately one-seventh of its value erect and compensatory fluid shifts occur. Sjöstrand studied five male subjects and found that an average of 643 ml of blood or approximately 11% of the average blood volume was shifted from the lower extremities to the rest of the body during recumbency (ref. 4). Of this blood 78% was taken up by the thorax. The diuresis associated with recumbency is well known and is discussed in detail in a recent review of salt and water volume receptor mechanisms (ref. 5). Basett et al. in 1924 confirmed the observation that a dilute urine may be excreted on a subject's assuming the recumbent posture (ref. 6). Hulet and Smith have stated that the recumbency diuresis in hydropenic subjects is principally an osmotic diuresis related to the increased excretion of sodium (ref. 7). Thomas has suggested that recumbency may stimulate an extracellular fluid volume receptor mechanism which, by decreasing aldosterone secretion by the adrenals, would decrease sodium reabsorption by the renal tubules (ref. 8). Such volume receptor mechanisms have recently been identified for the reflex regulation of aldosterone secretion (ref. 9). Citing evidence for cardiac atrial volume receptor mechanisms, Henry et al. note that, in general, all procedures associated with increased filling of the intrathoracic circulation —— including recumbency, immersion, and negative pressure breathing —— are accompanied by an increased rate of urine flow. They present evidence for reflex inhibition of the antidiuretic hormone (ADH) by increased filling of the left atrium, with a resulting diuresis (ref. 10). This mechanism is now accepted as the Henry-Gauer reflex (ref. 5). Smith has stated that this mechanism is a reasonable explanation of the free-water diuresis of recumbency (ref. 5).

In the water-immersion situation the hydrostatic pressure effects of the circulatory system are largely neutralized by ambient water pressure. Circulatory compensation for postural change is no longer required. Epstein noted that the diuresis of recumbency tends to persist when the subject assumes the erect posture in water (ref. 3). Gowenlock et al. report that, although sodium excretion decreases considerably while the subject stands in air after recumbency, there is no change while he stands in water after recumbency (ref. 11). Aldosterone excretion decreases when the subject is recumbent and when he stands in water but increases when he stands in air (ref. 11).

A pronounced diuresis has been observed consistently during immersion of human subjects in water. This was first described in detail by Basett et al. in 1924 (ref. 6) and was noted during the water-immersion experiments done by Graveline et al. (ref. 12). In the latter experiment a diuresis began soon after immersion and after 6 to 12 hours was accompanied by a demanding polydipsia. This phase lasted for about 72 hours at which time hematocrit values of 57 and 58 were noted. The diuresis was associated with a simultaneous increase in urinary nitrogen excretion. Following this 72-hour period the diuresis abruptly subsided to near control levels of urine flow, and hematocrit and urinary nitrogen excretion values returned to normal. A diuresis is known to be associated with negative pressure breathing (ref. 10). Initially, this was believed to be the mechanism for the observed immersion diuresis, for an element of negative pressure breathing does exist in head-out water immersion, as the water pressure applied to the chest is greater than the atmospheric pressure in the airway.

A further study by Graveline and Jackson was designed to investigate the mechanisms of the diuretic response to complete immersion with unrestricted activity and pressure-compensated or neutral respiration (ref. 13). An aviator's partial-pressure helmet with a modified SCUBA regulator was used to counter ambient water pressure. In such experiments the diuresis still occurred. In 5 subjects the effects of a 6-hour period of complete water immersion on urine flow, solute excretion, hematocrit, serum solutes, and renal function were studied (ref. 13). Osmolar clearances, the urine-to-plasma osmolar ratio, and free-water clearances were determined for the 5 subjects during 6-hour nonimmersed control periods and during immersion. There was an increase in osmolar clearances during immersion reflecting an increased solute excretion, particularly of urea and sodium. However, during immersion all subjects demonstrated a decrease in the urine-to-plasma osmolar ratio and the free-water clearance tended to become positive. A mean increase in an estimated GFR of about 75% occurred during immersion.

Although the diuretic response to immersion is qualitatively identical to the recumbency diuresis, whether the increased sodium excretion and the diuresis of water immersion may be ascribed to volume receptor mechanisms or altered renal hemodynamics or both remains to be determined. Increased free-water clearance during immersion suggests that the diuresis is due in part to antidiuretic hormone (ADH) suppression as in recumbency. Urinary urea excretion is consistently elevated during the water-immersion diuresis. Whether the urea originated from muscle tissue under the relative disuse conditions of immersion or whether it was "flushed out" of the renal medullary interstitium by the increased rate of urine flow also remains to be determined.

The diuresis of recumbency is transient and self-limiting within an hour (ref. 7). However, in studies of water immersion, it is significant that the observed diuresis is relatively persistent or nonadapting (refs. 6, 13, 14). In recent studies on the diuresis of negative pressure breathing, breathing periods varying from 30 minutes to 2 hours were used (refs. 10, 15, 16). However, in Beckman's studies of head-out immersion the diuretic response persisted for 12 to 23 hours (ref. 14). In the investigation reported by Graveline et al. the diuretic effect of water immersion persisted for 3 days, at which time urine flow returned to preimmersion control levels (ref. 12). In the case of water immersion the postulated reflex inhibition of ADH apparently persists for some hours unlike recumbency and continuous negative pressure breathing in which the urine flow may return to control levels after 60 to 90 minutes despite continuation of the stimulus. A result of the persistent diuretic response in the water-immersion studies has been a tendency to hemoconcentration and dehydration.

No clear-cut mechanisms can be suggested to explain the phenomenon of nonadaptation or persistence of the diuresis of immersion. Left atrial volume receptors may be stimulated either by a persistent increase in central venous blood volume (ref. 10) or by continuous distortion as in "pulsatile" pressure breathing (ref. 17). Nothing is known of the adaptation of atrial stretch receptors. A relative decrease in osmotically active muscle tissue components due to decreased muscle activity may occur during immersion with loss of muscle tissue water into the extracellular fluid, including the vascular compartment (ref. 18). The role of continued high levels of urinary nitrogen excretion as an osmotic diuretic must also be considered. Finally, the effect of the altered proprioceptive input to the central nervous system produced by water immersion on specific reflex systems such as ADH inhibition is unknown.

The body fluid response to changes in posture and to immersion appears to be related to hydrostatic pressure effects due to gravity and suggests the possibility that, in zero-G, an initial redistribution of body fluids may be expected with a compensatory diuretic response. In programming future manned space flights attention must be given to the possible effects of weightlessness on the state of hydration, and astronauts should be prepared to note and correct fluid deficits if they occur. ADH is known to inhibit the diuresis of recumbency (refs. 5, 14) and immersion (ref. 19), and could be administered if necessary.

A limited amount of information pertinent to body fluid physiology is currently available from our manned orbital space flights. This data must be interpreted with caution. However, certain trends are apparent, particularly in the second U. S. manned orbital flight (refs. 19, 20). This astronaut experienced a substantial decrease in body weight during the mission, and his urine collection bag contained 2360 cc of urine with specific gravity 1.003. It is evident from the weight change that fluid output exceeded intake by a large amount and relative dehydration resulted. Several known factors contributed to this response. Primary among them was a problem with recurrent increased suit inlet temperature with overheating and sweating. However, the physiologically intriguing observation is that during this flight a large amount of very dilute urine was excreted. This inappropriate urinary response is compatible with significant and protracted ADH suppression. A similar trend seems to be evident from the first manned orbital flight but is much less striking (ref. 21).

IV. LIST OF REFERENCES

1. Thompson, W.O., P.K. Thompson, and M.E. Daily, "The Effect of Posture upon the Composition and Volume of Blood in Man," J. of Clin. Invest. 5:573, 1927.

2. Waterfield, R.L., "The Effects of Posture on the Circulating Blood Volume," J. of Physiol. 72:110, 1931.

3. Epstein, F.H., A.V.N. Goodyer, F.D. Lawrason, and A.S. Relman, "Studies of the Antidiuresis of Quiet Standing," J. of Clin. Invest. 30:63, 1951.

4. Sjöstrand, T., "Volume and Distribution of Blood and Their Significance in Regulating the Circulation," Physiol. Rev. 33:202, 1953.

5. Smith, H.W., "Salt and Water Volume Receptors," Am. J. Med. 23:623, 1957.

6. Basett, H.C., S. Thurlow, C. Crowell, and W. Stewart, "Studies on the Effects of Baths on Man," Am. J. Physiol. 70:430, 1924.

7. Hulet, W.H., and H.W. Smith, "Postural Naturesis and Urine Osmotic Concentration in Hydropenic Subjects," Am. J. Med. 30:8, 1961.

8. Thomas, S., "Some Effects of Change of Posture on Water and Electrolyte Excretion by the Human Kidney," J. of Physiol. 139:337, 1957.

9. Anderson, C.H., M. McCally, and G.L. Farrell, "The Effects of Atrial Stretch on Aldosterone Secretion," Endocrinology 64:202, 1959.

10. Gauer, O.H., J.P. Henry, and H.O. Sieker, "Cardiac Receptors and Fluid Volume Control," Prog. In Cardiovasc. Dis. 4:1, 1961.

11. Gowenlock, A.H., J.W. Mills, and S. Thomas, "Acute Postural Changes and Aldosterone and Electrolyte Excretion in Man," J. of Physiol. 146:133, 1959.

12. Graveline, D.E., B. Balke, R.E. McKenzie, and B. Hartman, "Psychobiologic Effects of Water-Immersion-Induced Hypodynamics," Aerospace Med. 32:387, 1961.

13. Graveline, D.E., and Margaret M. Jackson, "Diuresis Associated with Prolonged Water Immersion," J. Appl. Physiol. 17:519, 1962.

14. Beckman, E.L., K.R. Coburn, R.M. Chambers, R.E. DeForest, W.S. Augerson, and V.G. Benson, "Physiologic Changes Observed in Human Subjects during Zero G Simulation by Immersion in Water up to the Neck Level," Aerospace Med. 32:1031, 1961.

15. Boylan, J.W., and D.E. Antkowiak, "Mechanism of Diuresis during Negative-Pressure Breathing," J. Appl. Physiol. 14:116, 1959.

16. Surtshin, A., J. Hoeltzenbein, and H.L. White, "Some Effects of Negative Pressure Breathing on Urine Excretion," Am. J. Physiol. 180:612, 1955.

17. Love, A.H.G., R.A. Roddie, J. Rosenweld, and R.G. Shanks, "Effect of Pressure Changes in Respired Air on Renal Excretion of Water and Electrolyte," Clin. Sci. 16:281, 1957.

18. Dill, D.B., J.H. Talbott, and H.T. Edwards, "Studies in Muscular Activity, VI. Response of Several Individuals to a Fixed Task," J. of Physiol. 69:267, 1930.

19. Graveline, D.E., and M. McCally, "Body Fluid Distribution: Implications for Zero Gravity," Aerospace Med. 33:1281, 1962.

20. Results of the Second United States Manned Orbital Space Flight, May 24, 1962, NASA SP-6, Manned Spacecraft Center, National Aeronautics and Space Administration, U.S. Government Printing Office, Washington 25, D.C., 1962.

21. Results of the First United States Manned Orbital Space Flight, February 20, 1962, Manned Spacecraft Center, National Aeronautics and Space Administration, U.S. Government Printing Office, Washington 25, D.C., 1962.

V. CARDIOVASCULAR DECONDITIONING

Early workers in aviation medicine speculated that heart failure would occur within minutes of a pilot's initial exposure to weightlessness (ref. 1). These fears have been dispelled by the lack of demonstrable cardiovascular alteration in orbiting animals and man (refs. 2-5). More recently it has been proposed that exposure to prolonged weightlessness might result in disuse deterioration of cardiac musculature (ref. 6). This seems unlikely, as the major physical elements of stroke work —— inertia of the blood, viscosity of the blood, and the elastic resistance of the vascular system —— will be largely unaltered in the absence of gravity.

The assuming of erect posture by primates has resulted in the evolution of certain adaptive mechanisms which counteract the effect of gravitational force upon the circulating blood. Without such homeostatic devices to prevent the pooling of blood in the dependent portions of the body, cardiac output and the flow of blood to the brain would be impaired by any gravitational or accelerative force applied in the vertical axis. Study of the anti-G mechanisms of the cardiovascular system has provided much of our basic knowledge of cardiovascular dynamics and reflexes. Reconsideration of this material is germane to a discussion of the possible physiological consequences of the absence of gravity. Excellent reviews are available (refs. 7, 8).

In the erect posture the major large arteries and veins are oriented parallel to the gravitational field and significant hydrostatic pressures are produced in these long uninterrupted columns of blood. Within 30 minutes of quiet standing (refs. 8, 9, 10), 400 to 500 cc. of plasma may pool in the vascular and interstitial spaces of the legs. The arterial, capillary, and venous pressures are markedly elevated in the dependent extremities and the circulatory system must make appropriate compensation to insure an adequate venous return and cardiac output.

Anti-G compensatory mechanisms include: (a) the effect of extravascular or tissue pressure: a definite relationship between low intramuscular pressure in the legs and syncope has been demonstrated by Mayerson and Burch (ref. 11), (b) the muscle pump of the legs, (c) the abdominothoracic pump mechanism, (d) the return of unabsorbed capillary filtrate to the circulation by the lymphatics, (e) vasoconstriction of the splanchnic and dependent vascular beds, and (f) cardioacceleration.

The normal cardiodynamic responses to vertical posture have been studied many times (refs. 7, 8, 9, 10, 11, 12, 13). A reduction in stroke volume is observed in human subjects on their assuming the erect posture. The heart rate is slightly accelerated but the net effect is a transient diminution in cardiac output (refs. 7, 8, 12). The systolic blood pressure remains the same or falls slightly, the diastolic rises, and the pulse pressure narrows. Pulmonary blood volume, heart size, and central venous pressure are reduced (refs. 7, 8, 13). When the hydrostatic pressure gradients of the cardiovascular system are largely nullified during the immersion of erect subjects in water, cardiodynamic measurements remain those characteristic of recumbency (refs. 14, 15).

When the cardiovascular compensations for the erect posture fail for some reason, syncope or fainting results. Syncope or fainting represents the failure of the cardiovascular system to maintain adequate arterial perfusion of the brain. Syncope is of two general types: vasodepressor or vasovagal syncope (the common faint) and that associated with the relatively uncommon clinical disorder of postural hypotension. Vasodepressor syncope can be elicited experimentally by passively tilting normal subjects into the erect position (ref. 16). The incidence and rate of onset of syncope during tilt may be increased by venesection, venous occlusive tourniquets, vasodilator drugs, or prior exercise or immobilization.

Vasodepressor or vasovagal syncope during tilt is characterized by a relative bradycardia, nausea, pallor, sweating, dizziness, dimming of vision, and an abrupt fall in blood pressure, and represents a vagotonic discharge superimposed on the basic sympathetic response to the orthostatic stress. The trigger mechanism for the vagotonic discharge is unknown, but the increased cholinergic activity is probably the primary mechanism in the faint (refs. 17, 18). Reflex peripheral vasodilation as evidenced by a sudden increase in extremity blood flow has been described during vasodepressor syncope on the tilt table (ref. 18). Because syncope occurs most commonly in the erect posture and is promptly relieved by lying down, many investigators have attributed this phenomenon to reduced cardiac output resulting from the bradycardia and pooling of blood in the dependent extremities. However, prevention of the bradycardia with atropine does not affect the fall in blood pressure in the fainting reaction (ref. 17). Also, cardiac catheterization studies have demonstrated a reduction in right atrial pressure and cardiac output following passive tilting, while at the onset of a fainting reaction blood pressure falls with no further drop in cardiac output (ref. 19). Obviously syncope can result from any combination of the factors which reduce heart rate, stroke volume, or peripheral resistance (ref. 10).

The clinical disorder known as postural hypotension or chronic orthostatic hypotension may be idiopathic or may be secondary to diabetes, tabes dorsalis, Addison's disease, or syringomyelia. The idiopathic variety, itself uncommon, is usually noted as a triad of anhidrosis, impotence, and chronic orthostatic hypotension and probably represents a basic disturbance in sympathetic innervation, possibly in the hypothalamus (ref. 20). Stead and Ebert have shown that patients with chronic orthostatic hypotension do not pool more blood in the lower portion of the body than do normal subjects, but that normal pooling causes an abnormal fall in blood pressure due to an absence or deficiency in reflex arteriolar and venous constriction (ref. 21). In contrast to vasodepressor syncope, the faint of postural hypotension represents an apparent failure of reflex sympathetic vasoconstriction and is characterized by the absence of the signs and symptoms of vagotonic discharge.

Orthostatic intolerance with tachycardia, narrowing of the pulse pressure, pallor, sweating, and an increased incidence of fainting develops in normal subjects during vertical tilt following as little as 1 week of bed rest (ref. 22) or 12 hours of complete water immersion (ref. 23). In both bed rest and water immersion the hydrostatic pressure effects of the blood due to gravity are minimal or absent. Deprived of their necessary stimulus, cardiovascular postural reflexes become deconditioned by disuse. Similarly, in a weightlessness environment there will be no hydrostatic pressure effects and therefore no demand on cardiovascular postural reflexes. Cardiovascular deconditioning with orthostatic intolerance of the same type as produced by bed rest and water immersion may well be expected as a consequence of prolonged exposure to weightlessness.

The mechanisms of the postural hypotension that develops during prolonged inactivity in bed rest (ref. 22) or water immersion (refs. 23, 24) are complex and as yet incompletely defined. Deitrick, Whedon, and Shorr noted that orthostatic intolerance on the tilt table, with a marked tendency to fainting, developed in healthy male subjects within one week of the onset of strict bed rest (ref. 22). Leg circumference during tilt was significantly greater during the bed rest period, suggesting that a major defect is excessive pooling of blood in the dependent extremities due to impaired venous or muscular tone. The occurrence of purpuric hemorrhages about the feet and ankles during the tilt was thought to be evidence of increased capillary fragility and possibly permeability. Blood volume is also known to decrease progressively for the first 2 to 3 weeks of prolonged bed rest in spite of its initial augmentation due to recumbency (refs. 22, 25), and may contribute to subsequent orthostatic intolerance.

The vasoconstrictor response of sympathetic stimulation is mediated by the liberation of norepinephrine at postganglionic nerve endings. The urinary excretion of norepinephrine in normal subjects increases over threefold when the subject is tilted to 75° (ref. 26). The orthostatic tachycardia and increase in diastolic blood pressure measured when a subject is tilted after bed rest and water immersion suggest that reflex sympathetic vasoconstriction is not impaired (refs. 22, 23). However, urinary norepinephrine excretion is diminished during recumbency (ref. 26) and during water immersion (ref. 27), presumably reflecting decreased vasomotor activity. Patients with chronic orthostatic hypotension have high normal plasma (ref. 28) and low 24-hour urine levels of norepinephrine (ref. 29) and fail to demonstrate the normal increase in plasma and urinary norepinephrine with passive tilt (refs. 28, 29). The role of the sympathetic catecholamines in the cardiovascular deconditioning of bed rest and water immersion remains to be determined.

Attention has recently been directed to volume sensitive receptors within the thorax. There is now good evidence that the secretion of both ADH and aldosterone are regulated in part by volume distention of the cardiac atria (refs. 30, 31). Augmentation of central blood volume results in the inhibition of ADH and a free-water diuresis and decreased secretion of aldosterone with a resulting increased sodium excretion. The redistribution of fluid and electrolyte resulting from inactivity, recumbency, and immersion has been discussed. The mechanical properties of blood-vessel walls depend to a degree on the water and electrolyte content of their smooth muscle. In a recent review Tobian (ref. 32) suggested that the water and ion concentration in vascular walls may regulate the vascular reactivity of blood vessels, particularly small vessels and arterioles.

The effects of immersion on body fluids and electrolytes and the resulting orthostatic intolerance might then be explained in part as follows: immersion with its attendant inactivity results in a shift of blood volume distribution centrally with a resulting diuresis and naturesis. Over a period of time there is a decrease in circulating blood volume, cumulative electrolyte imbalance, and loss of body water. Such complex changes could alter vascular reactivity and account, in part, for the observed orthostatic hypotension and diminished acceleration tolerance seen following immersion. Further studies are required to confirm such speculations and to define the mechanisms of fluid, electrolyte, and vascular reflex alterations which occur during recumbency and immersion, particularly the roles of ADH, aldosterone, and the catecholamines.

Physical conditioning is another important factor in cardiovascular metabolism and performance. Morris in a large statistical study of British workers suggests an inverse relationship between the degree of physical activity and mortality from coronary heart disease (ref. 33). Clinical evidence of existing atherosclerosis appeared higher in 300 middle-aged sedentary individuals as compared with a similar number of athletes of the same age (ref. 34).

Eckstein has noted an augmentation of the coronary vascular bed in exercised dogs (ref. 35). The beneficial effects of appropriate levels of exercise are now being emphasized (refs. 33, 34, 36, 37).

Raab has commented extensively on the significance of disuse for the myocardium, stressing the relative "cholinergic" preponderance of trained athletes and the potentially harmful consequences of the "adrenergic" preponderance of sedentary individuals (refs. 36, 37). The athlete, as a rule, shows highly developed vagal tone: bradycardia at rest, relatively slight cardioacceleration with stress with rapid deceleration after the stress, a long isometric contraction period, and the absence of hypoxic changes on the ECG during severe exertion. The "loafer's" heart is characterized by adrenergic preponderance: a tendency to resting tachycardia, marked and prolonged cardiac acceleration with relatively mild exertion, ECG changes of hypoxia, and reduced cardiac efficiency with strenuous exercise (ref. 37). All of these features resemble those elicited by the administration of epinephrine and norepinephrine or by cardiac sympathetic stimulation. Bed rest produces similar cardiac adrenergic preponderance (ref. 38).

The exact metabolic mechanisms whereby disuse produces a shift towards adrenergic preponderance is unknown. The heart muscle absorbs and stores catecholamines from the circulating blood (ref. 37), but information is lacking regarding the synthesis, release, rate of turnover, and tissue levels of catecholamines in relation to level of training or use.

In a zero-G environment, with relative inactivity and absence of hydrostatic pressure effects, a redistribution of body fluids and a loss of cardiovascular reflex anti-G mechanisms may occur. This loss of reflex cardiovascular adaptability may be considered a problem in deconditioning or adaptation of the organism to a less demanding environment (refs. 23, 39). The length of time of exposure necessary to produce adaptive changes that might impair an astronaut's ability to withstand the acceleration of reentry or other cardiovascular stress will only be determined with experience and experimentation in space. There is no available evidence of impaired reentry tolerance of American or Russian astronauts.

Presuming that cardiovascular deconditioning similar to that produced with bed rest will be a function of some unknown time exposure to weightlessness, there are two general approaches to the problem of the prevention of unwanted effects.

The first is to prevent the occurrence of adaptive changes. The most obvious method is by using artificial gravity. Whedon, Deitrick, and Shorr demonstrated that the metabolic abnormalities of bed rest were reduced by one-half, and that the loss of cardiovascular postural mechanisms was largely prevented by the use of passive exercise in an oscillating bed (ref. 40). The responsible stimulus provided by the oscillation —— mild muscular exercise, weight bearing, or hydrostatic pressure effects —— is unknown and should be determined. Graveline simulated the hydrostatic pressure effects of gravity by inflating four extremity venous tourniquets repetitively during immersion and completely prevented the orthostatic intolerance to tilt demonstrated by the subjects immersed without the tourniquets (ref. 24). Positive pressure breathing or repeated Valsalva maneuvers might prevent the postulated blood volume shifts of zero-G and help to prevent cardiovascular deconditioning. This procedure might also be of value in preventing the atelectasis which is reported to occur in high oxygen content atmospheres (ref. 41).

A second general technique is to protect the subject after adaptive changes have occurred by preventing dependent pooling of blood with elastic wrappings or a counterpressure garment as in the treatment of orthostatic hypotension (ref. 10). The use of sympathomimetic drugs, mineralocorticoids, and angiotensin should not be considered until a better understanding of the neurohormonal mechanisms of orthostatic intolerance is obtained.

V. LIST OF REFERENCES

1. Langer, E., in von Diringshofen, "Wie wird sich der Menschliche Organismus voraussichtlich in schwere Freien Raum verhalten?" (What is the Probable Behavior of the Human Organism in Gravity-Free Space?), Weltraumfahrt 4:81, 1951.

2. Burch, G.E., and S.J. Gerathewohl, "Some Observations on Heart Rate and Cardiodynamics during Weightlessness," Aerospace Med. 31:661, 1960.

3. Beischer, D.C., and A.R. Fregly (Editors), Animals and Man in Space. A Chronology and Annotated Bibliography through the Year 1960, ONR Report ACR-64, Office of Naval Research, Washington, D.C., 1960.

4. Henry, J.P., E.R. Maher, and D.G. Simons, "Animal Studies of the Sub-Gravity State during Rocket Flight," J. Aviat. Med. 23:421, 1952.

5. Henry, J.P., "Effects of Weightlessness in Ballistic and Orbital Flight: A Progress Report," Aerospace Med. 33:1056, 1962.

6. Stutman, L.J., and R. Olson, "Effects of Zero Gravity upon the Cardiovascular System," Armed Forces Med. J. 11:1162, 1960.

7. Hellebrandt, F.A., and E.B. Franseen, "Physiological Study of the Vertical Stance of Man," Physiol. Rev. 23:220, 1943.

8. Rushmer, R.F., "Effects of Posture," Cardiovascular Dynamics, Chap. 7, W.B. Saunders Co., New York, 1961.

9. Thompson, W.O., P.K. Thompson, and M.E. Daily, "The Effect of Posture upon the Composition and Volume of Blood in Man," J. Clin. Invest. 5:573, 1927.

10. Wayne, H.H., "Syncope: Physiological Considerations and an Analysis of the Clinical Characteristics in 510 Patients," Am. J. Med. 30:418, 1961.

11. Mayerson, H.S., and G.E. Burch, "Relationships of Tissue (Subcutaneous and Intramuscular) and Venous Pressures to Syncope Induced in Man by Gravity," Amer. J. Physiol. 128:258, 1940.

12. Stead, E.A., Jr., J.V. Warren, A.J. Merrill, and E.S. Brannon, "The Cardiac Output in Male Subjects as Measured by the Technique of Right Atrial Catheterization. Normal Values with Observations on the Effect of Anxiety and Tilting," J. Clin. Invest. 24:326, 1945.

13. Sjöstrand, T., "Volume and Distribution of Blood and Their Significance in Regulating the Circulation," Physiol. Rev. 33:202, 1953.

14. Erlanger, J., and D.R. Hooker, "An Experimental Study of Blood Pressure and of Pulse Pressure in Man," Johns Hopkins Hosp. Reps. 12:145, 1904.

15. Hellebrandt, F.A., and E. Brogdon, "The Hydrostatic Effect of Gravity on the Circulation in Supported, Unsupported and Suspended Postures," Am. J. Physiol. 123:95, 1938.

16. Allen, S.C., C.L. Taylor, and V.E. Hall, "A Study of Orthostatic Insufficiency by the Tiltboard Method," Am. J. Physiol. 143:11, 1945.

17. Stead, E.A., "Fainting," Am. J. Med. 13:387, 1952.

18. Brigden, W., S. Howarth, and E.B. Sharpey-Schafer, "Postural Changes in Peripheral Blood Flow of Normal Subjects with Observations on Vasovagal Fainting Reactions as a Result of Tilting, the Lordotic Posture, Pregnancy and Spinal Anesthesia," Clin. Sc. 9:79, 1950.

19. Weissler, A.M., J.J. Leonard, and J.V. Warren, "Effects of Posture and Atropine on the Cardiac Output," J. Clin. Invest. 36:1656, 1957.

20. Friedberg, C.K., Diseases of the Heart, 2nd Edition, p. 313, W.B. Saunders Co., Philadelphia, 1956.

21. Stead, E.A., and R. Ebert, "Postural Hypotension; A Disease of the Sympathetic Nervous System," Arch. Int. Med. 67:546, 1941.

22. Deitrick, J.E., G.D. Whedon, and E. Shorr, "The Effects of Immobilization on Various Metabolic and Physiologic Functions of Normal Men," Am. J. Med. 4:3, 1948.

23. Graveline, D.E., and G.W. Barnard, "Physiologic Effects of a Hypodynamic Environment: Short-Term Studies," Aerospace Med. 32:726, 1961.

24. Graveline, D.E., "Maintenance of Cardiovascular Adaptability during Prolonged Weightlessness," Aerospace Med. 33:297, 1962.

25. Taylor, H.L., L. Erickson, A. Henschel, and A. Keys, "The Effect of Bed Rest on the Blood Volume of Normal Young Men," Am. J. Physiol. 144:227, 1945.

26. Sundin, T., "The Influence of Body Posture on the Urinary Excretion of Adrenaline and Noradrenaline," Acta. Med. Scandinav. (Suppl.) 161:336, 1958.

27. McCally, M., and D.E. Graveline, Urinary Catecholamine Response to Water Immersion, AMRL-TDR-63-20, 6570th Aerospace Medical Research Laboratories, Aerospace Medical Division, Wright-Patterson Air Force Base, Ohio, March 1963.

28. Hickler, R.B., R.E. Wells, H.R. Tyler, and J.T. Hamlin, III, "Plasma Catecholamine and Electro-Encephalographic Responses to Acute Postural Change. Evidence of a Deficient Pressor Amine Response in Postural Hypotension," Am. J. Med. 26:410, 1959.

29. Luft, R., and U.S. von Euler, "Two Cases of Postural Hypotension Showing a Deficiency in Release of Nor-Epinephrine and Epinephrine," J. Clin. Invest. 32:1065, 1953.

30. Gauer, O.H., J.P. Henry, and H.O. Sieker, "Cardiac Receptors and Fluid Volume Control," Prog. in Cardiovasc. Dis. 4:1, 1961.

31. Farrell, G., and A.N. Taylor, "Neuroendocrine Aspects of Blood Volume Regulation," Ann. Rev. Physiol. 24:471, 1962.

32. Tobian, L.,"Interrelationship of Electrolytes, Juxtaglomerular Cells and Hypertension," Physiol. Rev. 40:280, 1960.

33. Morris, J.N., and M.D. Crawford, "Coronary Heart Disease and Physical Activity of Work," Brit. Med. J. 2:1485, 1958.

34. Wolffe, J.B., "Continued Vigorous Physical Activity as a Possible Factor in the Prevention of Atherosclerosis," Circulation 16:517, 1957.

35. Eckstein, R.W., "Effect of Exercise and Coronary Arterial Narrowing on the Growth of Interarterial Coronary Anastomoses," Fed. Proc. 15:34, 1956.

36. Raab, W., "Loafer's Heart," Arch Int. Med. 101:194, 1958.

37. Raab, W., P. Silva, H. Marchet, E. Kimura, and Y.K. Starcheska, "Cardiac Adrenergic Preponderance due to Lack of Physical Exercise and its Pathogenic Implications," Am. J. Cardiol. 5:300, 1960.

38. Taylor, H.L., A. Henschel, J. Brozek, and A. Keys, "Effects of Bed Rest on Cardiovascular Function and Work Performance," J. Appl. Physiol. 2:223, 1949.

39. Reynolds, S.R.M., "Sensory Deprivation, Weightlessness and Anti-Gravity Mechanisms. The Problem of Fetal Adaptation to a Floating Existence," Aerospace Med. 32:1061, 1961.

40. Whedon, D.G., J.E. Deitrick, and E. Shorr, "Modification of the Effects of Immobilization upon Metabolic and Physiologic Functions of Normal Man by the Use of an Oscillating Bed," Am. J. Med. 6:684, 1949.

41. Comroe, J.H., Jr., R.D. Drips, P.R. Dumke, and M. Deming, "Oxygen Toxicity, the Effect of Inhalation of High Concentrations of Oxygen for Twenty-Four Hours on Normal Man at Sea Level and at a Simulated Altitude of 18,000 Feet," J. Am. Med. Assoc. 128:710, 1945.

VI. MUSCLE ATROPHY

The dependence of muscle strength and muscle mass on use or exercise is obvious to anyone who has had an extremity immobilized in a plaster cast. The possibility of muscular weakness and atrophy occurring during weightlessness has been discussed (refs. 1, 2, 3).

The consequences of the disuse and immobilization of muscle include: loss of muscle mass, increased excretion of nitrogen, altered creatine metabolism, weakness, impaired exercise tolerance, and loss of support for leg veins (refs. 4, 5). Evidence of such catabolic and deteriorative processes has led to recent criticism of bed rest as a therapeutic tool and to the present vogue of early postoperative ambulation (ref. 6).

The mechanisms of muscle atrophy have been studied extensively with particular regard to the trophic influence of the nervous system on nonnervous tissue (refs. 7, 8, 9). It is important to distinguish between the results of simple disuse of muscle and of nerve section (refs. 8, 9). Reid sectioned the spinal cord at L4 and at S2, cut the dorsal roots bilaterally, and cut the ventral roots on one side (ref. 8). On the completely denervated side reflexes were absent, the strength-duration curve was abnormal, and fibrillation and atrophy occurred. On the disused side with its motor roots intact the reflexes were absent but spontaneous motion occurred. Fibrillation was absent and the strength-duration curve was normal. The muscle mass on the disused side was markedly decreased due to a decrease in the volume of sarcoplasm. Nerve section produces pronounced and rapid muscle degeneration whereas simple disuse atrophy proceeds slowly (ref. 9).

Electromyographic studies have demonstrated that normal resting muscle exhibits no neuromuscular activity, contrary to widespread belief that there is random activity of motor units in a resting muscle to provide what is called muscular tone (ref. 10). According to Basmajian, muscular tone is simply the responsiveness of muscle tissue to the nervous system (ref. 10). Fudema et al. have shown that the electromyographic response to a constant percutaneous supramaximal stimulus to the peroneal nerve declines steadily in an immobilized limb over a 100-day period and that the amplitude of the motor unit potential decreases similarly (ref. 11). Both innervation and activity are required for the maintenance of normal form and function in muscle.

Following 7 days of water immersion, Graveline et al. noted a marked decrease in work capacity on the treadmill, marked subjective weakness, and increased nitrogen excretion in their single subject (ref. 2).

In the 2-week immersion study of Graybiel and Clark, however, muscle strength was fully maintained and work capacity on the treadmill was reduced only moderately in 2 of 3 subjects (ref. 1). These subjects were immersed for 10 hours each day and spent the remaining hours at bed rest. The authors suggest that the small amount of exercise in getting out of the water and moving in bed may have been a sufficient stimulus to maintain normal strength.

Recent studies have emphasized the importance of daily muscular training and brief maximal exercise in maintaining strength (refs. 12, 13). Mueller and Hettinger found that exercise constitutes a training stimulus to a muscle if it exceeds one-third of that muscle's potential maximal strength (ref. 12). An increase in muscle strength generally will result, even if the total daily activity of the muscle is markedly reduced. There is a rapid decline in strength on the cessation of exercise but a high muscular potential (50% to 80% over the initial strength) can be maintained by maximum contractions once a week. Rose et al. were able to demonstrate that plateau strength of the quadriceps femoris may be maintained by a brief (5-second) maximal isotonic exercise as seldom as once monthly (ref. 13). Such brief maximal efforts may not represent muscular exercise in the sense in which it is traditionally regarded but may rather be a manifestation of the persistence of strength as a learned act (ref. 14).

The mass and strength of most large muscle groups can apparently be maintained by brief maximal exercise of the isometric type. However, certain anti-G muscles and tissues such as the intercostal, paraspinous, pelvic, and cervical muscle groups, intervertebral discs, and joint ligaments may undergo disuse during weightlessness and may not be exercised by conventional regimens. Care must be taken to evaluate the condition of tissues whose only function is anti-G and whose deterioration may not be readily apparent in the weightlessness environment. For example, the role of the musculoskeletal system in human acceleration tolerance and the muscle groups involved has not been well defined and might be an important factor in reentry tolerance.

Muscle atrophy is not likely to be a serious problem in space flight unless the crew is severely restrained. Joint resistive chairs and suits or other bulky or power-consuming exercise units may not be necessary although elastic or spring devices to simulate the musculoskeletal effects of the erect posture on earth must be considered. However, only experience in space will enable us to dissociate musculoskeletal alterations due to weightlessness from those due to the inactivity of cabin confinement and to determine the duration of exposure necessary to induce significant musculoskeletal changes.

VI. REFERENCES

1. Graybiel, A., and B. Clark, "Symptoms Resulting from Prolonged Immersion in Water. The Problem of Zero G Asthenia," Aerospace Med. 32:181, 1961.

2. Graveline, D.E., B. Balke, R.E. McKenzie, and B. Hartman, "Psychobiological Effects of Water-Immersion-Induced Hypodynamics," Aerospace Med. 32:387, 1961.

3. Potts, P., and J.I. Bowring, "Exercise in a Weightless Environment," Physical Therapy Rev. 40:584, 1960.

4. Deitrick, J.E., G.D. Whedon, and E. Shorr, "The Effects of Immobilization on Various Metabolic and Physiologic Functions of Normal Men," Am. J. Med. 4:3, 1948.

5. Keys, A., Conference on Metabolic Aspects of Convalescence, pp. 90-92, Josiah Macy, Jr., Foundation, Boston, Mass., 1944.

6. Dock, W., "The Undesirable Effects of Bed Rest," Surg. Clin. North America, 25:437, 1945.

7. Tower, S.S., "The Reaction of Muscle to Denervation," Physiol. Rev. 19:1, 1939.

8. Reid, G., "A Comparison of the Effects of Disuse and Denervation upon Skeletal Muscle," Med. J. Australia 2:165, 1941.

9. Chor, H., and R.E. Dolkart, "A Study of 'Simple Disuse Atrophy' in the Monkey," Am. J. Physiol. 117:626, 1936.

10. Basmajian, J.V., "Electromyography of Postural Muscles," in F.G. Evans (editor), Biomechanical Studies of the Musculoskeletal System, C.C. Thomas, Springfield, Ill., 1961.

11. Fudema, J.J., J.A. Fizzell, and E.M. Nelson, "Electromyography of Experimentally-Immobilized Skeletal Muscles in Cats," Am. J. Physiol. 200:963, 1961.

12. Mueller, E.A., and T. Hettinger, "Die bedeutung des trainengsverlaufes für die trainengstetigkeit von muskeln" (The Importance of the Training Program for Muscle Performance), Arbeitphysiol. 15:452, 1954.

13. Rose, D.L., S.F. Radzyminski, and R.R. Beatty, "Effect of Brief Maximal Exercise on the Strength of the Quadriceps Femoris," Arch. Phys. Med. 38:157, 1957.

14. Helebrandt, F.A., and S.J. Houtz, "Mechanisms of Muscle Training in Man, Experimental Demonstration of the Overload Principle," Phys. Therapy. Rev. 36:371, 1956.

VII. DISUSE OSTEOPOROSIS

The normal skeletal bone mass results from a metabolic steady state in which the rate of bone formation equals that of bone destruction. Bone formation consists of two processes: formation of the bone matrix, principally protein and mucopolysaccaride, and the deposition in this matrix of the bone mineral, apatite, which is principally calcium and phosphorus. Bone destruction or osteoclastic activity is a single process in which both protein and mineral are removed. The isolated decalcification of bone does not occur. Diminution in bone mass may result from either increased bone resorption or decreased bone formation. Increased bone resorption is characteristic of hyperparathyroidism (osteitis fibrosa cystica). Decreased bone formation may represent a failure to deposit apatite (osteomalacia) or underactivity of the osteoblasts in producing bone matrix (osteoporosis). The complex physiology of calcium, parathyroid hormone, citric acid, and vitamin D in the metabolism of bone has been recently reviewed (refs. 1, 2, 3, 4).

Osteoporosis is a condition in which bone mass is decreased as the result of a decrease in the rate of bone matrix formation, and is a disorder of protein rather than calcium or phosphorus metabolism (ref. 5). Osteoporosis may be classified as congenital, senile, nutritional, endocrine, idiopathic, and disuse. Disuse osteoporosis may be localized to immobilized parts of the skeleton, while all other forms have a generalized distribution. Because the osteoporosis of disuse is a disorder of bone matrix and not of calcium and phorphorus metabolism per se, the serum calcium, phosphorus, and phosphatase levels are generally normal. Serum calcium and phosphorus levels would not reveal the occurrence of disuse osteoporosis as a consequence of weightlessness. Serial urine calcium or radioactive calcium turnover determinations in a calcium balance situation are necessary for such a study.

The maintenance of normal skeletal metabolism is dependent on mechanical forces such as those produced by weightbearing and muscle tension. When these forces are decreased or removed, bone mass decreases and osteoporosis results. Osteoporosis can be produced experimentally by plaster immobilization (ref. 6), tenotomy (ref. 7), and denervation (ref. 8). In general, the bone atrophy is proportional to the degree of disuse. Mechanical factors stimulate osteoblastic activity and the absence of mechanical strain leads to diminished osteoblastic activity and a net reduction in bone formation (refs. 9, 10). Bell (ref. 9) and Whedon (ref. 10) have critically reviewed the clinical and laboratory observations that have established beyond doubt that disuse is associated with bone atrophy.

Considerable controversy exists regarding the exact mechanisms of the bone atrophy of disuse (ref. 9). Direct evidence for the dependence of osteoblastic activity on the mechanical strain of bone is lacking. From radioactive calcium turnover and calcium balance studies of paralyzed

subjects with acutely developing disuse osteoporosis, Heaney concluded that the bone atrophy is due chiefly to an increased rate of bone resorption rather than failure of bone formation (ref. 11). Whether disuse osteoporosis is mediated directly by the absence of mechanical strain or indirectly by alterations in vascularity (ref. 7) or a hormonal imbalance is as yet unknown.

The immobilization of normal human subjects in bivalved body casts for periods of up to 7 weeks did not produce radiographically significant osteoporosis (ref. 12). Such immobilization produced prompt and gradually increasing excretion of calcium, both urinary and fecal, which was maximal at 4 to 5 weeks. Calcium losses were approximately one-half as great when the same subjects were tilted slowly from the horizontal to 20° down every 2 minutes during the immobilization (ref. 13).

Whedon and Shorr have reported that, in the immobilization produced by acute paralytic anterior poliomyelitis, changes occur in bone and calcium metabolism similar to those in normal subjects immobilized in plaster, but the former are more marked (ref. 14). X-ray evidence of osteoporosis was seen within 8 to 9 weeks after the onset of the disease. This increased rate of bone atrophy may relate to the more rigorous immobilization of flaccid paralysis or to the effects of motor denervation itself. In paralyzed subjects mechanical strain of bone produced by mobilization or by passive tilt does not influence the extent or duration of negative calcium balance (refs. 14, 15). However, Abramson studied two groups of paraplegics: one confined to wheelchairs and the other walking with braces for 1 hour daily. This study showed that the weightbearing group had less osteoporosis of the legs and pelvis as determined by X-ray (ref. 16).

Wyse and Pattee attempted to separate the effects of local vascular change, weightbearing, and muscle contraction in the genesis of disuse osteoporosis in paraplegics using the oscillating bed and the tilt table (ref. 15). They concluded that muscle contraction is the principal stimulus to osteoblastic activity.

In the absence of the mechanical strain of bone, disuse osteoporosis can occur and would be a logical consequence of prolonged passive exposure to weightlessness. The degree of osteoporosis due to weightlessness will depend entirely on the level of activity or programmed exercise in any given spacecraft configuration. The minimal strain stimulus necessary to maintain normal bone structure is unknown. If significant disuse does occur as a complication of inactivity and weightlessness, present knowledge of bone metabolism suggests that simple muscle exercise which provides mechanical strain on bones will prevent bone atrophy. Isometric contractions induced by faradic stimulation of immobilized muscles reduce the bone rarefaction (ref. 7). The electrical stimulation of motor points should be considered if it becomes necessary to prevent muscle atrophy and disuse osteoporosis during prolonged weightlessness.

The high incidence of renal tract calculus formation in immobilized patients has been related to increased calcium excretion (refs. 17, 18). Calculus formation is a complex process involving the metabolism and urinary excretion of calcium, phosphate, and citrate, urine volume and pH, diet, and urinary tract microbiology. However, if increased calcium excretion occurs as a consequence of prolonged weightlessness, consideration must be given to the prevention of renal calculi (ref. 19).

VII. REFERENCES

1. Nicolaysen, R., N. Eeg-Larsen, and O.J. Malm, "Physiology of Calcium Metabolism," Physiol. Rev. 33:424, 1953.

2. Rasmussen, H., "Parathyroid Hormone: Nature and Mechanism of Action," Am. J. Med. 30:112, 1961.

3. Harrison, H.E., "The Interrelationship of Citrate and Calcium Metabolism," Am. J. Med. 20:1, 1956.

4. Neuman, W., and Neuman, M., "Emerging Concepts of the Structure and Metabolic Functions of Bone," Am. J. Med. 22:123, 1957.

5. Bartter, F.C., "Osteoporosis," Am. J. Med. 22:797, 1957.

6. Allison, N., and B. Brooks, "Bone Atrophy: An Experimental and Clinical Study of the Changes in Bone which Result from Non-Use," Surg. Gynec. and Obst. 33:250, 1921.

7. Geiser, M., and J. Trueta, "Muscle Action, Bone Rarefaction and Bone Formation: An Experimental Study," J. Bone and Joint Surg. 40-B:282, 1958.

8. Carbin, K.B., and J.C. Hinsey, "Influence of the Nervous System on Bones and Joints," Anat. Rec. 75:307, 1939.

9. Bell, G.H., "Bone as a Mechanical Engineering Problem," in G.H. Bourne (editor), Biochemistry and Physiology of Bone, Academic Press, New York, 1956.

10. Whedon, G.D., "Osteoporosis; Atrophy of Disuse," in K. Rodahl, J.T. Nicholson, and E.M. Brown, Jr. (editors), Bone as a Tissue, McGraw-Hill Book Co., New York, 1960.

11. Heaney, R.P., "Radiocalcium Metabolism in Disuse Osteoporosis in Man," Am. J. Med. 33:188, 1962.

12. Deitrick, J.E., G.D. Whedon, and E. Shorr, "Effects of Immobilization on Various Metabolic and Physiologic Functions of Normal Men," Am. J. Med. 4:3, 1948.

13. Whedon, G.D., J.E. Deitrick, and E. Shorr, "Modification of the Effects of Immobilization upon the Metabolic Functions of Normal Men by the Use of an Oscillating Bed," Am. J. Med. 6:684, 1949.

14. Whedon, G.D., and E. Shorr, "Metabolic Studies in Paralytic Acute Anterior Poliomyelitis," J. Clin. Invest. 36:966, 1957.

15. Wyse, D.M., and C.J. Pattee, "Effect of the Oscillating Bed and Tilt Table on Calcium, Phosphorus and Nitrogen Metabolism in Paraplegia," Am. J. Med. 17:645, 1954.

16. Abramson, A.S., "Bone Disturbances in Injuries to the Spinal Cord and Cauda Equina: Their Prevention by Ambulation," J. Bone and Joint Surg. 30:982, 1948.

17. Kimbrough, J.C., and J.C. Denslow, "Urinary Tract Calculi in Recumbent Patients," J. Urol. 61:837, 1949.

18. Leadbetter, W.F., and H.C. Engster, "The Problems of Renal Lithiasis in Convalescent Patients," J. Urol. 53:269, 1945.

19. Cockett, A.T.K., C.C. Beehler, and J.E. Roberts, Hypodynamic Urolithiasis: A Potential Hazard during Prolonged Weightlessness in Space Travel, School of Aerospace Medicine, Review 2-62, Brooks Air Force Base, Texas, December 1961.

VIII. SENSORY REACTIONS

Sensory reactions to weightlessness include a number of related subjects, some of which have been discussed in detail in the literature (refs. 1-15). Otolith and vestibular function in the weightlessness state have been studied in the pioneer work of Haber (ref. 1), Gerathewohl (ref. 2), Ballinger (ref. 3), von Beckh (ref. 4), and Graybiel (ref. 5). The effects of weightlessness on orientation and psychomotor performance have been reviewed by Loftus and Hammer (ref. 6) and by Henry et al. (ref. 7). These reports suggest that, as long as vision is present, no serious disorientation occurs and psychomotor tasks can be performed in weightlessness with proficiency for many hours or even days.

If a rotating vehicle is used to provide artificial gravity, autonomic symptoms, nystagmus, the oculogyral illusion, and disorientation due to Coriolis acceleration effects may occur. However, studies performed in the slow-rotation room at the U.S. Naval School of Aviation Medicine by Graybiel and his coworkers suggest that prolonged constant rotation, within some ranges studied, does not interfere with gross task performance (ref. 8). Motivation and performance may be affected by a type of motion sickness (canal sickness) due to unusual stimulation of the semicircular canals by head motion. From studies of the time course of adaptation to the oculogyral illusion (ref. 9) and of conditioned compensatory nystagmus (ref. 10), Graybiel has suggested that human subjects can adapt to the vestibular stimulation of a rotating environment. That vestibular habituation is possible is indicated by the study of dancers and skaters who have reduced nystagmus and sensation in an unusual acceleration environment (ref. 11).

The psychological effects of space flight include the fear and anxiety of real physical danger. These factors have not been significant operational problems to date (ref. 7). Ruff (ref. 12) and Levy, Ruff, and Thaler (ref. 13) have suggested that prolonged isolation and confinement in a hostile environment combined with prolonged weightlessness may produce psychological effects similar to those seen in laboratory studies of isolation and sensory deprivation. Such laboratory studies have established that, if the quantity and quality of sensory input is low, disturbances in perception and thought will occur (ref. 14). Lilly has suggested that proprioceptive feedback from muscles and joints may be particularly important for normal mental activity (ref. 15).

The concept that homeostatic regulatory mechanisms depend on sensory input to the nervous system has been recognized in part since the time of Sherrington (ref. 16). This concept has recently been set forth in the terms of modern control theory by D. and K. Stanley-Jones in their book, The Kybernetics of Natural Systems, in which the roles of positive and negative feedback in a wide range of biological systems are reviewed

(ref. 17). Feedback systems, synonymous in part with sensory input, stabilize physiological systems and prevent runaway to maximum or minimum. Several studies of lower animals and man (refs. 17, 18) attest to the importance of proprioceptive input in the physiological regulation of respiration (ref. 19), orthostatic tolerance (ref. 20), posture (ref. 16), and cerebral electrocortical activity (ref. 21). The positive stereotropism of young animals (refs. 17, 18) and the "contact comfort" of young monkeys reported by Harlow (ref. 22) may also be examples of the homeostatic importance of proprioception.

For a variety of populations the magnitude of stimulus-produced activation of the autonomic nervous system is, in general, related negatively to the prestimulation level of physiological function (refs. 23, 24). This concept has been derived mathematically as the Law of Initial Values (ref. 24). Therefore, an autonomic reflex or physiological response with a low level of prestimulation excitation will show a high level of reactivity upon stimulation.

MacLean and Allen in 1940 described two cases of postural hypotension associated with tachycardia and noted that the symptoms were worse on arising in the morning and much improved by evening and were dramatically alleviated by the use of a head-up bed (ref. 25). They postulated that some factor associated with recumbency was responsible for the observed loss of adaptation. Graveline has suggested that the loss of adaptation of the cardiovascular system to the hydrostatic pressure effects of gravity seen following bed rest and water immersion may also be related to alterations in the pattern or quantity of afferent cardiovascular reflex impulses (ref. 26). Similar mechanisms have been postulated for the free-water diuresis of water immersion (ref. 27), and for the apparently inappropriate excretion of a relatively large amount of dilute urine by the astronaut of the second U.S. manned orbital space flight (ref. 28). Such interpretations of the role of proprioceptive sensory input are, at the present time, highly speculative.

A limited amount of data pertinent to sensory reactions in weightlessness is available from the orbital space flights of animals and man (refs. 6, 7). Gazenko in a discussion of the Russian bioastronautic results noted a number of physiological findings which were interpreted as indicating a certain instability of the central nervous systems regulating vegetative function (ref. 29). In the orbital experiment with the dog Laika, the heart rate returned to normal in the weightlessness state approximately three times more slowly than after the same accelerations in the laboratory. The stability of the heart rate was decreased as measured by the difference of the maximum and minimum values of the R-R interval of the ECG for 10-second intervals. The depth and frequency of respirations were also noticeably nonuniform. Similar instability, though less pronounced, was noted in cosmonaut Gagarin's electroencephalogram. The possibility was suggested that these phenomena were caused by

altered function of the sensory receptor apparatus in the weightlessness state. No similar data has been reported from Project Mercury (ref. 7).

The central nervous system is constantly receiving a great variety of sensory information from the body and its environment. The interaction of these numerous afferent systems is the basis of the functional state of the central nervous system or the "neural dynamic" as it has been termed (ref. 17). The concept of the interaction of afferent nervous systems has been developed by the Russian, L.A. Orbelli (ref. 30). In the weightlessness state, the input from a variety of receptors, particularly proprioceptive and vestibular, will be altered as the adequate gravitational stimulus decreases or disappears. The as-yet-unanswered questions are: how essential are the consequences of such deafferentiation, and how and when will they show themselves?

VIII. REFERENCES

1. Haber, H., and S.J. Gerathewohl, "Physics and Psychophysics of Weightlessness," J. Aviat. Med. 22:180, 1951.

2. Gerathewohl, S.J., "Personal Experiences during Short Periods of Weightlessness Reported by Sixteen Subjects," Astronautica Acta. 4:204, 1956.

3. Ballinger, E.R., "Human Experiments in Subgravity and Prolonged Acceleration," J. Aviat. Med. 23:319, 1952.

4. von Beckh, H.J.A., "Experiments with Animals and Human Subjects under Sub and Zero Gravity Conditions during the Dive and Parabolic Flight," J. Aviat. Med. 25:235, 1954.

5. Graybiel, A., and J.L. Patterson, "Thresholds of Stimulation of the Otolith Organs as Indicated by the Oculogravic Illusion," J. Appl. Physiol. 7:666, 1955.

6. Loftus, J.P., and Lois R. Hammer, Weightlessness and Performance: A Review of the Literature, ASD TR 61-166, Aeronautical Systems Division, Wright-Patterson Air Force Base, Ohio, June 1961.

7. Henry, J.P., "Effects of Weightlessness in Ballistic and Orbital Flight. A Progress Report," Aerospace Med. 33:1056, 1962.

8. Clark, B., and A. Graybiel, "Human Performance during Adaptation to Stress in the Pensacola Slow Rotation Room," Aerospace Med. 32:93, 1961.

9. Graybiel, A., F.E. Guedry, W. Johnson, and R. Kennedy, "Adaptation to Bizarre Stimulation of the Semi-Circular Canals as Indicated by the Oculogyral Illusion," Aerospace Med. 32:321, 1961.

10. Guedry, F.E., Jr., and A. Graybiel, "Compensatory Nystagmus Conditioned during Adaptation to Living in a Rotating Room," J. Appl. Physiol. 17:398, 1962.

11. McCabe, B.F., and M. Lawrence, "Suppression of Vestibular Sequelae Following Rapid Rotation," J. Aviat. Med. 30:194, 1959.

12. Ruff, G.E., "Psychological Effect of Space Flight," Aerospace Med. 32:639, 1961.

13. Levy, E.Z., G.E. Ruff, and V.H. Thaler, "Studies in Human Isolation," J. Amer. Med. Assoc. 169:236, 1959.

14. Solomon, P., P.H. Leiderman, J. Mendelson, and D. Wexler, "Sensory Deprivation: A Review," Amer. J. Psychiat. 114:357, 1957.

15. Lilly, J.C., "Mental Effects of Physical Restraint and of Reduction of Ordinary Levels of Physical Stimuli on Intact Healthy Persons," Psychiat. Res. Rep. 5:1, 1956.

16. Sherrington, C.S., The Integrative Action of the Nervous System, Yale University Press, New Haven, Conn., 1906.

17. Stanley-Jones, D. and K., The Kybernetics of Natural Systems, Pergamon Press, New York, 1960.

18. Milne, L.J. and M., The Senses of Animals and Man, Atheneum, New York, 1962.

19. Comroe, J.H., and C.F. Schmidt, "Respiratory Reflexes from the Limbs," Fed. Proc. 1:16, 1942.

20. Graveline, D.E., and G.W. Barnard, "Physiologic Effects of a Hypodynamic Environment: Short-Term Studies," Aerospace Med. 32:726, 1961.

21. Hodes, R., "Electrocortical Synchronization in Cats from Reduction of Proprioceptive Drive Caused by a Muscle Relaxant," Fed. Proc. 20:332, 1961.

22. Harlow, H.F., and R.R. Zimmerman, "Affectional Responses in the Infant Monkey," Science. 130:421, 1959.

23. Lacey, J.I., and Beatrice C. Lacey, "The Relationship of Resting Autonomic Activity to Motor Impulsivity," in Solomon, Cobb, and Penfield (editors), The Brain and Human Behavior, Williams and Wilkins Co., Baltimore, Md., 1958.

24. Lacey, J.I., "The Evaluation of Autonomic Responses: Toward a General Solution," Ann. N.Y. Acad. of Sci. 67:123, 1956.

25. MacLean, A.R., and E.V. Allen, "Orthostic Hypotension and Orthostatic Tachycardia. Treatment with the Headup Bed," J. Amer. Med. Assoc. 115:2162, 1940.

26. Graveline, D.E., "Maintenance of Cardiovascular Adaptability during Prolonged Weightlessness," Aerospace Med. 33:297, 1962.

27. Graveline, D.E., and Margaret M. Jackson, "Diuresis Associated with Prolonged Water Immersion," J. Appl. Physiol. 17:519, 1962.

28. Graveline, D.E., and M. McCally, "Body Fluid Distribution: Implications for Zero Gravity," Aerospace Med. 33:1281, 1962.

29. Gazenko, O.G., and V.I. Yadovsky, "Some Results of Physiological Reactions to Space Flight Conditions," Paper read at American Rocket Society meeting, December 1961, The Academy of Sciences of USSR, Vol I, Moscow, 1961.

30. Orbelli, L.A., Problems of High Nervous Activity, The Academy of Sciences of the USSR, Moscow, 1949.

IX. CONCLUSIONS AND RECOMMENDATIONS

Serious consideration must be given to the disuse and deconditioning aspects of prolonged human exposure to weightlessness. Disuse changes can only be defined in the space environment, their time course determined, and protective techniques evaluated. An extensive biosatellite program will be expensive and much basic work must be done in the laboratory with bed rest, immobilization, immersion, and cabin-confinement techniques.

The time course of adaptive changes during zero-G and sub-G will determine man's performance capability in space or on lunar stations, the length of space duty tours, and vehicle design criteria, and may be a decisive factor in the ponderous decision on the necessity for artificial gravity by rotation of the vehicle of a given operation.

For this reason the passive exposure to weightlessness of suitably instrumented animals for 5, 10, 20, or 30 days or longer would be a critical experiment. Although the technical problems of orbiting, maintaining, and recovering an experimental animal for such periods are many, such a project is entirely feasible at the present time. The collection of biomedical data in space deserves separate consideration from the operational problems of a manned space program. Biomedical data cannot be meaningfully collected simply as an addendum to another space mission.

Biomedical data may be collected in space in any of a variety of configurations. Automatically instrumented biosatellites are presently feasible. If the in-flight collection of biological samples is not effective, before-and-after flight testing of physiological functions of test animals would still justify such experiments. In the Gemini capsule one astronaut could collect biological specimens and perform medical tests on the second passenger who might be a well-instrumented chimpanzee. A rotating biomedical satellite would allow the study of human subjects in fractions of G, dependent on the subject's distance from the craft's axis of rotation, for significant periods of time.

It would be desirable to collect biomedical data from a number of physiological systems. Cardiovascular reflex adaptability, particularly as it affects human acceleration tolerance, must be studied before and after incremental zero-G exposures. Electrocardiographic, blood pressure, heart rate, ballistocardiographic or vibrocardiographic, venous plethysmographic, and urine and serum catecholamine responses must be determined during zero-G and post-zero-G orthostatic and acceleration testing. Drugs, hormones, venous tourniquets, G-suits, repetitive Valsalva maneuvers, and intermittent positive pressure breathing must be evaluated as cardioprotective techniques.

Alterations in body fluid distribution in both zero-G and sub-G must be quantitated to define their magnitude and operational significance. Appropriate studies would include quantitative analysis of urine, blood volume, and body fluid compartment measurements, pertinent hormone assays (aldosterone and antidiuretic hormone), and renal function tests.

At least two efforts are needed in the study of musculoskeletal function. First, metabolic and performance functions related to the musculoskeletal system must be studied as a function of exposure time to zero-G or sub-G. In-space facilities for metabolic balance studies with controlled activity and environmental conditions, as well as equipment for testing musculoskeletal mass and strength, must be available. Simple measurements of muscle girth, electromyographic recording equipment, and spring ergometers for strength testing should be included. Second, exercise techniques and devices must be selected which most adequately maintain musculoskeletal function as determined by metabolic and performance criteria. Calcium, phosphorus, nitrogen, sulfur and citrate metabolism, creatine tolerance, X-ray bone densitometry, and serum enzyme levels should be appropriately studied.

The relation of altered sensory input to sleep, level of awareness, and vigilance must be established inflight by electroencephalographic, electrooculographic, electromyographic, biochemical, and performance data. The identification of disorders of vestibular origin, such as that suggested by cosmonaut Titov's "spacesickness," must be made during space flight. Primate subjects with loss of their semicircular canals, their otolith apparatus, or both might be studied during flight with a variety of motion stimuli. A sufficient number of controlled observations of man and animals must be obtained to establish the incidence and time course of symptomatology of any vestibular disorder. The completion of such studies establishing the mechanisms and prevention of canal sickness is prerequisite to the optimum design of rotating vehicles.

Respiratory gas exchange, gastrointestinal motility and absorption, urinary bladder function, adrenal cortical secretion, and other functions not apparently altered by short periods of weightlessness must be observed for alterations due to prolonged exposure.

Most important of all, we need information regarding the interaction of the multiple stresses of space flight. The effect of prolonged weightlessness on any particular physiological system must be considered in relation to other simultaneous or sequential environmental factors such as confinement and inactivity, transient accelerations, respiratory gases of artificial composition and pressure, radiation, and fatigue. This information obviously can come only from biomedical observation in the space flight environment.

X. SUMMARY

Some of the problems in physiology posed by prolonged weightlessness have been discussed in detail in this paper. The information needed and possible methods for its acquisition have been discussed. There are no clear guidelines to which problems most urgently need study and what are reasonable priorities for the biomedical study of weightlessness in space. For instance, the drainage of the nasal sinuses may prove to be a more significant problem in prolonged weightlessness than cardiovascular deconditioning or muscle atrophy. We can only assume that, as data accumulates from incremental manned space flight and, hopefully, animal biosatellites, any area of significant physiological change or disability will become apparent. Suitable tests, instrumentation, and experimental design could then be fed, ideally, into an existing biomedical satellite program and the area in question studied in detail.

Aerospace Medical Division,
6570th Aerospace Medical Research
Laboratories, Wright-Patterson AFB, Ohio.
Rpt. No. AMRL-TDR-63-3. THE PATHO-
PHYSIOLOGY OF DISUSE AND THE PROBLEM OF
PROLONGED WEIGHTLESSNESS: A REVIEW.
Final report, Jun 63, iv + 46 pp., 169 refs.
Unclassified report

The physiological implications of zero-G as encountered in space flight are discussed and the available research concerning the physiological effects of weightlessness is reviewed. The purpose of this review is to proceed from the present state of knowledge of normal human physiological systems, particularly as their structure and

(over)

UNCLASSIFIED

1. Weightlessness
2. Pathophysiology
3. Water Immersion
4. Bed Rest

I. AFSC Project 7222, Task 722201

II. McCally, Michael Biomedical Laboratory, 6570th Aerospace Medical Research Laboratories

III. Lawton, Richard W. General Electric Co. Philadelphia, Pa.

UNCLASSIFIED

function are affected by gravity, to a consideration of the possible physiological consequences of prolonged human exposure to zero-G. Methods used to produce and to simulate zero-G are briefly reviewed. The data suggesting that prolonged weightlessness will be a deconditioning environment is presented. This data is considered for possible untoward effects of prolonged exposure to weightlessness, and for methods of prevention of undesired effects. The problem of artificial gravity by rotation of a space vehicle is briefly considered. Areas of needed future investigation are suggested.

UNCLASSIFIED

IV. In DDC collection

V. Aval fr OTS: $1.50

UNCLASSIFIED

Aerospace Medical Division,
6570th Aerospace Medical Research
Laboratories, Wright-Patterson AFB, Ohio.
Rpt. No. AMRL-TDR-63-3. THE PATHO-
PHYSIOLOGY OF DISUSE AND THE PROBLEM OF
PROLONGED WEIGHTLESSNESS: A REVIEW.
Final report, Jun 63, iv + 46 pp., 169 refs.
Unclassified report

The physiological implications of zero-G as encountered in space flight are discussed and the available research concerning the physiological effects of weightlessness is reviewed. The purpose of this review is to proceed from the present state of knowledge of normal human physiological systems, particularly as their structure and

(over)

UNCLASSIFIED

1. Weightlessness
2. Pathophysiology
3. Water Immersion
4. Bed Rest

I. AFSC Project 7222, Task 722201

II. McCally, Michael Biomedical Laboratory, 6570th Aerospace Medical Research Laboratories

III. Lawton, Richard W. General Electric Co. Philadelphia, Pa.

UNCLASSIFIED

function are affected by gravity, to a consideration of the possible physiological consequences of prolonged human exposure to zero-G. Methods used to produce and to simulate zero-G are briefly reviewed. The data suggesting that prolonged weightlessness will be a deconditioning environment is presented. This data is considered for possible untoward effects of prolonged exposure to weightlessness, and for methods of prevention of undesired effects. The problem of artificial gravity by rotation of a space vehicle is briefly considered. Areas of needed future investigation are suggested.

UNCLASSIFIED

IV. In DDC collection

V. Aval fr OTS: $1.50

UNCLASSIFIED